

### **REMARKS**

The Office Action dated January 21, 2005, has been carefully considered. Claims 1, 36, 68, 69, 74, 79, 98 and 99 have been amended. Claims 1-83, 98 and 99 are in this application.

The claims were rejected under 35 U.S.C. § 112 as indefinite in view of the alternative recitation of (or). The claims have been amended to obviate the Examiner's rejection.

Claim 1 has been amended to include that the liquid remains in constant contact with a gaseous phase. Support for this amendment is found throughout the specification and in particular, on page 3, lines 7-15 of the application.

The previously presented claims 1-83 were rejected under 35 U.S.C. § 103 as obvious in view of previously cited U.S. Patent No. 6,068,751 to Neukermans. Applicants submit that the teachings of this reference do not teach or suggest the invention defined by the present claims.

Applicants submit that the present invention comprises of a method of fluidic control which relies on the combination of thermocapillary forces and substrate chemical patterning. The thermocapillary forces applied to the liquid necessitate the use of temperature gradients oriented essentially parallel to a gas/liquid interface. This in turn requires that the interface be always in direct contact with a gaseous phase, such as the ambient atmosphere. Chemical patterning is used to laterally confine the flow by causing the liquid to be either attracted to (i.e., wetting or hydrophilic) or repelled from (i.e., non-wetting or hydrophobic) designated regions. The chemical patterning can be applied to flat or topologically textured substrates which may include indentations, grooves or ridges whose surfaces must nonetheless remain open to a gaseous phase such as the ambient atmosphere.

Neukermans discloses a microfluidic delivery system including a microfluidic valve for controlling a flow of fluid through an elongated capillary. The capillary is enclosed by a layer of malleable material. A blade is activated toward the malleable material to occlude the capillary thereby barring liquid from flowing into the capillary. The blade is retracted away from the malleable material to allow fluid to flow into the capillary. Pressure applied to a fluid reservoir urges liquid in the reservoir to flow along the capillary when the blade is in the retracted position. A reaction chamber coupled to the capillaries can be heated as required for a chemical process.

The Examiner stated that the heating of the liquid moves the fluid along the surfaces of the applied patent to Neukermans. Applicants submit that contrary to the Examiner's suggestion there is no movement of the fluid by heating in the Neukermans device. Rather, the method for enclosed fluidic control disclosed in Neukermans relies on reservoirs included in a pouch together with capillaries that supply fluids whose flow is controlled by movement of blades against a malleable surface. The blade action causes the malleable surface to occlude or introduce fluid into designated regions. The fluid is confined to an internal channel and the blade valves regulate the delivery and timing of liquid throughout a network. Accordingly, the liquid metering is strictly caused by the movement of the blades. The heating elements in Neukermans are only used to provide suitable reaction conditions. Thus, as Neukermans states in column 13, line 2+, by placing heaters above or beneath the pouch, the user can also heat a liquid sample. Neukermans describes the use of heaters only for controlling the overall temperature of a liquid mass confined to a specified site as a way of initiating chemical reactions like PCR, as described in col. 13, lines 25-53. Neukermans refers to such heated chambers as "reaction chambers" to clarify their intended use (col. 9, lines 20-40). All reaction chambers must be held at a uniform temperature. Neukermans describes the usefulness of maintaining even the external pistons in contact with the sealed enclosure at the same elevated temperature in order to enhance the temperature uniformity at each site. (See col. 13, line 48).

The Examiner indicates that col. 13, line 2 recites that a plurality of heaters (individually activated or as desired) 196 may be disposed above below or in both substrates of the "patterned" microfluidic device comprised of a plurality of substrates shown in Figures 11 and 11A and selectively actuated to control the movement of the fluid through a respective flow path. However, Applicants submit that Neukermans at col. 13, lines 25-34 teaches that temperature cycling is used for maintaining the processing temperatures between appropriate PCR temperatures T1 and T2. There is no teaching or suggestion that the temperature is used for preventing or promoting liquid migration. Since the liquid is never subjected to and never supports a temperature difference oriented essentially parallel to a gas-liquid interface, the plurality of heaters of Neukermans can never be used to generate thermocapillary flow along a respective flow path. Rather, Neukermans teaches that the liquid is shuttled back and forth in

between processing chambers by opening all valves and admitting liquid into either one or the other processing chambers at col. 13, lines 34-37. Accordingly, in Neukermans, liquid is shuttled from one site to another (which may be maintained at different overall temperatures as for PCR) by the action of mechanical blades and pistons, not thermocapillary stresses.

Further, in contrast to the invention defined by the present claims, Neukermans does not teach or suggest receiving liquid on a patterned surface having an open architecture in which the liquid remains in constant contact with a gaseous phase such as the ambient atmosphere. The claims of the present invention have been amended to specify such features of an "open architecture" and the presence of a liquid in constant contact with "a gaseous phase". In the present invention, the thermocapillary forces used to move the liquid necessitate application of temperature gradients oriented essentially parallel to the gas/liquid interface. This geometry in turn necessitates that the said interface be always in direct contact with a gaseous phase. Any method of fluidic actuation involving thermocapillary shear stresses fails completely in the absence of a gas-liquid interface that can support a thermal gradient essentially parallel to said interface. In contrast, Neukermans teaches interior flow of liquid within closed capillaries in which there is no constant contact with a gaseous phase and no parallel thermal gradients. As suggested, Applicants have considered the bolded teachings in the Examiner's Office Action but do not agree with the Examiner's assessment that selective actuation of the plurality of heaters 196 in the Neukermans patent "... prevents (no heat) or promotes (heating) migration of the liquid." Rather, nowhere is it disclosed or suggested in Neukermans that the application of heat is used for enforcing liquid flow. Instead, Neukermans states in col. 13, line 2+, that "by placing heaters above or beneath the pouch, the user can also heat a liquid sample, say for initiating a chemical reaction". Thus, the Neukermans heating process is intended to heat the entirety of an enclosed liquid mass so as to maintain thermal uniformity. However, the Neukermans heating process plays no role whatsoever in generating or controlling the flow of liquid. To the contrary, Neukermans teaches away from the present invention by teaching the design of a microfluidic valve for controlling the flow of a liquid through an elongated capillary that is enclosed along at least one surface by a layer of a malleable material. The squeeze and release action caused by a set of blades pressing against the malleable boundary causes the sealed conduit to open and

introduce fluid or to close and block fluid into designated regions. Plungers are also sometimes used to push liquid from selected enclosed reservoirs toward the malleable valves. The liquid is never subject to nor ever supports a temperature gradient oriented parallel or essentially parallel to a gas-liquid interface.

The Examiner also stated that thermocapillary shear stresses are present in all microfluidic devices and shear stresses are always present in a microfluidic device and heating or non-heating increases or decreases the shear stress effect. Applicants submit that thermocapillary shear stresses require the application of a thermal gradient oriented parallel or essentially parallel to a gas-liquid interface. Accordingly, since Neukermans does not provide a gas-liquid interface, Neukermans does not provide liquid flow by thermocapillary stresses. In contrast, the chemical patterning of the present invention allows the formation of a gas-liquid interface which can support a thermal gradient. Moreover, Neukermans does not teach or suggest liquid flow by thermocapillary stresses nor the combination of these stresses with substrate chemical patterning.

With regard to claims 70 and 71, Neukermans does not teach or suggest a method or device for dividing a stream of liquid including individually activating one or more heating elements. Accordingly, the invention defined by the present claims is not obvious in view of Neukermans.

With regard to claims 72 and 73, Neukermans does not teach or suggest a method or device for mixing two or more liquids including individually activating one or more heating elements.

Accordingly, the invention defined by the present claims is not obvious in view of Neukermans.

Claims 98 and 99 were rejected as obvious in view of pages 353-355 of "Thermocapillary Pumping of Discrete Drop in Microfabricated Analysis Devices" by Sammarco et al.

Sammarco et al. teach fluidic control within the interior of a rectangular capillary by heating one end of a liquid droplet via heaters embedded within a glass substrate. In order for this flow mechanism to work at all, the liquid droplet must be confined to an interior channel. As

soon as the droplet is no longer completely enclosed within a channel (for example by removing either the top, bottom or one side wall), then the flow mechanism fails to work altogether.

In contrast to the invention defined by the present claims, Sammarco et al. do not teach or suggest flow of a liquid by thermocapillary shear stresses. To the contrary, Sammarco et al. describe application of a thermal gradient oriented perpendicularly and not in parallel to the gas-liquid interfaces comprising the front and back ends of a liquid plug. The Sammarco et al. plug completely fills the cross-section of the capillary within which the liquid is shuttled. The gas-liquid interfaces are each maintained at a uniform temperature but the temperature at the back and front ends may differ from each other. When they differ, the liquid plug is shuttled within the capillary by perpendicular stresses (also called normal stresses or Laplace stresses) completely different than conditions effective for preventing or promoting migration by shear stresses (also called parallel stresses or thermocapillary stresses). Sammarco et al. induce a force known as a capillary pressure gradient, which is completely different than the thermocapillary shear stress described in the present invention. Unfortunately, Sammarco et al incorrectly used the words "thermocapillary forces" in some of their publications when referring to their method of fluidic actuation but their method of droplet propulsion is strictly controlled by forces oriented perpendicular and not parallel to the gas-liquid interfaces. Applicants submit that the knowledge required to specify the thermocapillary shear stresses of the present invention, including the temperature differences and thermal gradients used to provide thermocapillary shear stresses, cannot be derived from the Sammarco et al. invention and would not be evident to one of ordinary skill in the art.


Furthermore, Sammarco et al. do not teach or suggest receiving liquid on a patterned surface having an open architecture comprising one or more surface pathways being either (1) a flat topology with chemical patterning or (2) an indentation, ridge or groove having chemical patterning as defined by the present claims. In addition, Sammarco et al. do not teach or suggest storing the device in glycerol as defined by present claims 98 and 99. There is no teaching or suggestion of a sample storage nor of the use of glycerol for preserving hydrophilicity. Rather, Sammarco et al. refer only to the use of glycerol as one of a number of liquid samples for testing

the operation of their device. Accordingly, the invention defined by claims 98 and 99 is not obvious in view of Sammarco et al.

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

Dated: July 21, 2005

  
\_\_\_\_\_  
Diane Dunn McKay  
Reg. No. 34,586  
Attorney for Applicant

MATHEWS, SHEPHERD, McKAY & BRUNEAU, P.A.  
100 Thanet Circle, Suite 306  
Princeton, NJ 08540  
Tel: 609 924 8555  
Fax: 609 924 3036